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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,749	03/30/2005	Shunichi Kuroda	GRT/1035-579	1581

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ARLINGTON, VA 22203

EXAMINER
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PENG, BO

ART UNIT	PAPER NUMBER
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1648

MAIL DATE	DELIVERY MODE
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03/06/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/529,749	<b>Applicant(s)</b> KURODA ET AL.	
	<b>Examiner</b> BO PENG	<b>Art Unit</b> 1648	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 December 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,4 and 6-9 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,4 and 6-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12/7/07 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

1. This Office Action is in response to the amendment filed on December 7, 2007. Claims 2, 3 and 10 have been cancelled. Claims 1, 4 and 6-9 are pending and are considered in this Office action.

#### ***Foreign Priority***

2. Applicant's provision of foreign priority document Japan 2002-339925 filed on 22 November 2002 is acknowledged. It is noted, however, that English translation has not been provided. Therefore, it is not clear whether the foreign priority document provide written description for the instant claims. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. 112, first paragraph. Therefore, the priority date is deemed to be the filing date of the priority application PCT/JP03/15003 on 25 November, 2003.

#### ***Drawings***

3. **(Prior objection-withdrawn)** The objection to drawings **is withdrawn** in view of the amendment to the Brief Description of the Drawings

#### ***Claim Objection***

4. **(Prior objection- withdrawn)** The objection to Claim 1 **is withdrawn**.

***Claim Rejections - 35 USC § 112, first paragraph***

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5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. **(Prior rejection-maintained)** The rejection of Claims 1, 4 and 6-9 under 35 U.S.C. 112, first paragraph, as failing to comply with enablement requirement **is maintained** for the reason of record set forth in the Office action dated September 7, 2007, and for the reasons set forth below.

Response to Applicant's arguments:

7. Applicant argues that a person skilled in the art would readily appreciate from the original disclosure that the first protein comprises a hepatitis B virus surface-antigen protein (HBsAg) whose hepatocyte recognition site is modified to another bio-recognizing molecule and the second protein comprises a hepatitis B virus core-antigen protein (HBc) which interact with each other when the two proteins are co-expressed. Applicant further argues that it is a well-known fact to a person skilled in the art that the HBcAg protein forms a capsid structure. Therefore, it would not require undue experimentation for a person of skill in the art to make and use the claimed invention.

8. Applicant's arguments are considered but found not persuasive for the following reasons: First, the Applicant's arguments are not relevant to the claim. Claim 1 requires hollow nanoparticles comprising a first particle-forming protein HBsAg fused with another bio-recognizing molecule and a second particle-forming protein HBcAg, whereas Applicant argues that the specification teaches how to make an HBsAg protein comprising bFGF protein. Note

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that a person skilled in the art would not recognize that a fusion HBsAg/bFGF protein and a nanoparticle comprising HBsAg/bFGF is the same thing. With regard to Applicant's argument that "it is a well-known fact to a person skilled in the art that the HBcAg protein forms a capsid structure", Claim 1 requires nanoparticles comprising at least both HBsAg/bio-recognizing molecules and HBcAg, as shown in Figure 1 in the specification, not an HBc particle alone.

9. As discussed in the previous Office action, the specification fails to teach how to make the claimed nanoparticles. The specification does not show how the alleged nanoparticles that comprise two particle-forming proteins are formed after co-expressing HBsAg L-bFGF and HBc in yeast cells (See Para 15, the Office action dated 9/7/07). The prior art teaches that it is unpredictable to assemble a foreign protein or substance into a viral particle. For example, the prior art teaches that expression of HBsAg L protein does not form a nanoparticle. Shiosaki (1991) teaches that the production of HBsAg-HBcAg particles in yeast cells require co-expression of four structural genes of HBV encoding three envelope proteins (HBsAg S, M, L) and HBcAg (Entire document, particularly see Summary, pp 145-148, and Figures 2-5). Shiosaki shows that elimination of one of these four components abolished the ability to form HBsAg-HBcAg particles. Consistent with the teaching of the prior art, the specification has not shown the nanoparticles are formed, that comprise particle-forming proteins; specifically, HBsAg fused with another uncharacterized molecule and HBcAg, as alleged in the claims.

10. Moreover, Applicant's arguments do not encompass the scope of the claims. Claim 1 requires a nanoparticle comprising HBsAg that contains an uncharacterized bio-recognizing molecule and HBcAg. Since the specification has not explicitly defined what the alleged bio-recognizing molecules are, the alleged bio-recognizing molecules could be anything, such as

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proteins, chemical compounds, etc. However, Applicant has not pointed where the specification has provided teachings how to make an HBsAg nanoparticle comprising any molecules. Thus, Applicant's arguments do not encompass the scope of the claims.

11. Finally, the specification fails to teach how to use the alleged particle as a drug for treating any disease. Applicant has failed to address this point in response to the previous Office action. The specification provides little guidance regarding how to make either a broad range of nanoparticles, or their application as a drug for treating any disease.

12. For the reasons discussed above, it would require undue experimentation for one skilled in the art to make and use the claimed nanoparticles. Therefore, the rejection is maintained.

### ***Claim Rejections - 35 USC § 102***

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --  
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. **(Prior rejection-withdrawn)** The rejection of Claims 1 and 6-9 under 35 U.S.C. 102(b) as being anticipated by Shiosaki (1991; Gene 106:143-149, cited in IDS) **is withdrawn** in view of the amendment to the claims.

### ***Remarks***

15. No claim is allowed. Accordingly, THIS ACTION IS MADE FINAL. See MPEP

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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37

CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, Ph.D. can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Bo Peng/  
February 26, 2008

/Zachariah Lucas/  
Primary Examiner, Art Unit 1648